General

Guideline Title

KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease.

Bibliographic Source(s)

KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney Int Suppl. 2012 Dec;2(5):337-414. [453 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis 2004 May;43(5 Suppl 1):S1-290.

Recommendations

Major Recommendations

Definitions of the strength of recommendation (Level 1, Level 2, or Not Graded) and the quality of the supporting evidence (A-D) are provided at the end of the "Major Recommendations" field.

Lifestyle and Pharmacological Treatments for Lowering Blood Pressure in Chronic Kidney Disease (CKD) Non-dialysis-Dependent (ND) Patients

General Strategies

- Individualize blood pressure (BP) targets and agents according to age, co-existent cardiovascular disease and other co-morbidities, risk of progression of CKD, presence or absence of retinopathy (in CKD patients with diabetes) and tolerance of treatment. (Not Graded)
- Inquire about postural dizziness and check for postural hypotension regularly when treating CKD patient's with BP-lowering drugs. (Not Graded)

Lifestyle Modification

- Encourage lifestyle modification in patients with CKD to lower BP and improve long term cardiovascular and other outcomes:
  - The Work Group recommends achieving or maintaining a healthy weight (body mass index [BMI] 20 to 25). (1D)
  - The Work Group recommends lowering salt intake to <90 mmol (<2 g) per day of sodium (corresponding to 5 g of sodium chloride), unless contraindicated. (1C)
  - The Work Group recommends undertaking an exercise program compatible with cardiovascular health and tolerance, aiming for at

least 30 minutes 5 times per week. (1D)
- The Work Group suggests limiting alcohol intake to no more than two standard drinks per day for men and no more than one standard drink per day for women. (2D)

Blood Pressure Management in CKD ND Patients without Diabetes Mellitus

- The Work Group recommends that non-diabetic adults with CKD ND and urine albumin excretion <30 mg per 24 hours (or equivalent*) whose office BP is consistently >140 mm Hg systolic or >90 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤140 mm Hg systolic and ≤90 mm Hg diastolic. (1B)
- The Work Group suggests that non-diabetic adults with CKD ND and urine albumin excretion of 30 to 300 mg per 24 hours (or equivalent*) whose office BP is consistently >130 mm Hg systolic or >80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤130 mm Hg systolic and ≤80 mm Hg diastolic. (2D)
- The Work Group suggests that non-diabetic adults with CKD ND and urine albumin excretion >300 mg per 24 hours (or equivalent*) whose office BP is consistently >130 mm Hg systolic or >80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤130 mm Hg systolic and ≤ 80 mm Hg diastolic. (2C)
- The Work Group suggests that an angiotensin receptor blocker (ARB) or angiotensin converting enzyme inhibitor (ACE-I) be used in non-diabetic adults with CKD ND and urine albumin excretion of 30 to 300 mg per 24 hours (or equivalent*) in whom treatment with BP-lowering drugs is indicated. (2D)
- The Work Group recommends that an ARB or ACE-I be used in non-diabetic adults with CKD ND and urine albumin excretion >300 mg per 24 hours (or equivalent*) in whom treatment with BP-lowering drugs is indicated. (1B)

*Approximate equivalents for albumin excretion rate per 24 hours—expressed as protein excretion rate per 24 hours, albumin/creatinine ratio, protein/creatinine ratio, and protein reagent strip results—are given in Table 1, Chapter 1 in the original guideline document.

Blood Pressure Management in CKD ND Patients with Diabetes Mellitus

- The Work Group recommends that adults with diabetes and CKD ND with urine albumin excretion <30 mg per 24 hours (or equivalent*) whose office BP is consistently >140 mm Hg systolic or >90 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤140 mm Hg systolic and ≤90 mm Hg diastolic. (1B)
- The Work Group suggests that adults with diabetes and CKD ND with urine albumin excretion >30 mg per 24 hours (or equivalent*) whose office BP is consistently >130 mm Hg systolic or >80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤130 mm Hg systolic and ≤80 mm Hg diastolic. (2D)
- The Work Group suggests that an ARB or ACE-I be used in adults with diabetes and CKD ND with urine albumin excretion of 30 to 300 mg per 24 hours (or equivalent*). (2D)
- The Work Group recommends that an ARB or ACE-I be used in adults with diabetes and CKD ND with urine albumin excretion >300 mg per 24 hours (or equivalent*). (1B)

*Approximate equivalents for albumin excretion rate per 24 hours—expressed as protein excretion rate per 24 hours, albumin/creatinine ratio, protein/creatinine ratio, and protein reagent strip results—are given in Table 1, Chapter 1 in the original guideline document.

Blood Pressure Management in Kidney Transplant Recipients (Non–dialysis-Dependent CKD of Any Stage with a Kidney Transplant [CKD T])

- The Work Group suggests that adult kidney transplant recipients whose office BP is consistently >130 mm Hg systolic or >80 mm Hg diastolic be treated to maintain a BP that is consistently ≤130 mm Hg systolic and ≤80 mm Hg diastolic, irrespective of the level of urine albumin excretion. (2D)
- In adult kidney transplant recipients, choose a BP-lowering agent after taking into account the time after transplantation, use of calcineurin inhibitors, presence or absence of persistent albuminuria, and other co morbid conditions. (Not Graded)

Blood Pressure Management in Children with CKD ND

- The Work Group recommends that in children with CKD ND, BP-lowering treatment is started when BP is consistently above the 90th percentile for age, sex, and height. (1C)
- The Work Group suggests that in children with CKD ND (particularly those with proteinuria), BP is lowered to consistently achieve systolic and diastolic readings less than or equal to the 50th percentile for age, sex, and height, unless achieving these targets is limited by signs or symptoms of hypotension. (2D)
- The Work Group suggests that an ARB or ACE-I be used in children with CKD ND in whom treatment with BP-lowering drugs is indicated, irrespective of the level of proteinuria. (2D)

Blood Pressure Management in Elderly Persons with CKD ND

- Tailor BP treatment regimens in elderly patients with CKD ND by carefully considering age, co-morbidities and other therapies, with gradual escalation of treatment and close attention to adverse events related to BP treatment, including electrolyte disorders, acute deterioration in kidney function, orthostatic hypotension and drug side effects. (Not Graded)

Definitions:

Final Grade for Overall Quality of Evidence

Grade	Quality of Evidence	Meaning
A	High	The Work Group is confident that the true effect lies close to that of the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very Low	The estimate of effect is very uncertain, and often will be far from the truth.

Nomenclature and Description for Grading Recommendations

	Implications		
Grade[a]	**Patients**	**Clinicians**	**Policy**
Level 1 'The Work Group recommends'	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2 'The Work Group suggests'	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require debate and involvement of stakeholders before policy can be determined.

[a]The additional category 'Not Graded' was used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence. The most common examples include recommendations regarding monitoring intervals, counseling, and referral to other clinical specialists. The ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than Level 1 or 2 recommendations.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Chronic kidney disease, including:
  - Diabetic kidney disease
  - Nondiabetic kidney diseases
  - Kidney disease in the kidney transplant recipient

Other Disease/Condition(s) Addressed

- Diabetes mellitus
- Hypertension

Guideline Category

Management

Treatment

Clinical Specialty

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Nephrology

Pediatrics

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Nurses

Pharmacists

Physician Assistants

Physicians

Social Workers

Guideline Objective(s)

- To provide advice on the management of blood pressure (BP) in patients with non–dialysis-dependent chronic kidney disease (CKD ND)
- To assist the practitioner caring for patients with non-dialysis CKD and hypertension and to prevent deaths, cardiovascular disease (CVD) events, and progression to kidney failure while optimizing patients' quality of life
- To update the National Kidney Foundation's (NKF) *Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease*, which was based on evidence collected up to 2001, by incorporating the evidence gathered since then

Target Population

- Adults with non-dialysis-dependent chronic kidney disease (CKD ND) without diabetes mellitus
- Adults with CKD ND with diabetes mellitus
- Adults with CKD ND who have received a kidney transplant (CKD T)
- Children with CKD ND
- Elderly with CKD ND

Interventions and Practices Considered

1. Establishment of individualized target blood pressure (BP)
2. Inquiring about dizziness and postural hypotension when BP-lowering drugs are used
3. Lifestyle modification
    - Achieving/maintaining healthy body weight
    - Lowering salt intake
    - Exercise program
    - Limiting alcohol intake
4. Use of BP-lowering drugs:
    - Angiotensin converting enzyme inhibitors (ACE-Is)
    - Angiotensin receptor blockers (ARBs)
    - Other BP-lowering drugs or combinations (aldosterone antagonists, beta-blockers, calcium-channel blockers, diuretics)
5. Blood pressure management in patients without diabetes mellitus
6. Blood pressure management in patients with diabetes mellitus
7. Blood pressure management in kidney transplant recipients
8. Blood pressure management in children
9. Blood pressure management in the elderly

Major Outcomes Considered

- Mortality
- Cardiovascular mortality
- Cardiovascular events
- Kidney failure
- Composite including clinical events
- Doubling of serum creatinine (SCr) or halving of glomerular filtration rate (GFR)
- Proteinuria (categorical)
- Kidney function (continuous)
- Urine protein level (continuous)
- Adverse events: drug discontinuation or dose decrease, hyperkalemia, early rise of SCr or decrease of GFR

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The Work Group sought to build on the evidence base from the previous *KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease*. As the first search for the Kidney Disease Outcomes Quality Initiative (KDOQI) guideline was conducted in July 2002, the search for the current KDIGO Guideline included publications since January 2002. Search strategies were developed by the Evidence Review Team (ERT) with input from the Work Group. The text words or medical subject headings (MeSH) that were included are provided in Supplementary Appendix 1 online (see the "Availability of Companion Documents" field). Non-human studies and those focusing on dialysis, pregnancy, neonates, malignant hypertension, acute kidney injury, or drug pharmacology were excluded.

The MEDLINE, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews were searched by the ERT to capture all randomized controlled trials (RCTs) on the use of blood pressure (BP)-lowering agents in chronic kidney disease (CKD). The first search was conducted in November 2009 and was subsequently updated in April and August of 2010; the final update was done in January 2011. Additional focused searches were conducted to identify RCTs evaluating lifestyle interventions of salt restriction, weight loss, and diet and exercise in chronic kidney disease (CKD) and to look for reviews of adverse effects of anti-hypertensive agents. The ERT relied on Work Group members

to identify large, general population RCTs reporting on subgroup analyses based on CKD, glomerular filtration rate (GFR), or proteinuria status. Additional pertinent articles were added from the reference lists of Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) and relevant meta-analyses and systematic reviews (see Table 7 in the original guideline document). The search yield was also supplemented by articles provided by Work Group members through February 2012.

A total of 10,657 citations were initially screened. Journal articles reporting original data, meta-analyses, and systematic reviews were selected for evidence review. Editorials, letters, abstracts, unpublished reports, and articles published in non–peer-reviewed journals were not included. The Work Group also decided to exclude publications from journal supplements because of potential differences in the process of how they get solicited, selected, reviewed, and edited compared to peer-reviewed publications. *Post hoc* analyses were also excluded, however, after discussion with the Work Group, it was decided that exception would be made for post-trial observational follow-up reports from RCTs looking at BP targets as BP interventions may take longer time to influence outcomes. These studies were downgraded one level to designate that they are of lesser quality than the original RCT.

Limitations of Approach

Although the literature searches were intended to be comprehensive, they were not exhaustive. MEDLINE was the only database searched. Hand searches of journals were not performed, and review articles and textbook chapters were not systematically searched. However, important studies known to domain experts that were missed by the electronic literature searches were added to retrieved articles and reviewed by the Work Group.

Number of Source Documents

A total of 10,657 citations were initially screened, and 247 articles were retrieved. Data extraction was performed on 55 studies. The overall search yield along with the number of abstracts identified and articles reviewed for each topic are presented in Table 8 of the original guideline document.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Recommendations Assessment, Development and Evaluation (GRADE) System for Grading Quality of Evidence for an Outcome

Step 1: Starting Grade for Quality of Evidence Based on Study Design	
Randomized trials	High
Observational study	Low
Any other evidence	Very low
Step 2: Reduce Grade	
Study quality	-1 level if serious limitations -2 levels if very serious limitations
Consistency	-1 level if important inconsistency
Directness	-1 level if some uncertainty -2 levels if major uncertainty
Other	-1 level if sparse or imprecise data[c] -1 level if high probability of reporting bias
Step 3: Raise Grade	
Strength of association	+1 level if strong,[a] no plausible confounders +2 levels if very strong,[b] no major threats to validity
Other	+1 level if evidence of a dose–response gradient

	+1 level if all residual plausible confounders would have reduced the observed effect
Final Grade for Quality of Evidence and Definition	
High	Further research is unlikely to change confidence in the estimate of the effect
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect, and may change the estimate
Low	Further research is very likely to have an important impact on confidence in the estimate, and may change the estimate
Very low	Any estimate of effect is very uncertain

[a]Strong evidence of association is defined as 'significant relative risk (RR) of >2 (<0.5)' based on consistent evidence from two or more observational studies, with no plausible confounders.

[b]Very strong evidence of association is defined as 'significant RR of >5 (<0.2)' based on direct evidence with no major threats to validity.

[c]Sparse if there is only one study or if total N <100. Imprecise if there is a low event rate (0 or 1 event) in either arm or confidence interval spanning a range <0.5 to >2.0.

Adapted by permission from Macmillan Publishers Ltd, *Kidney International*. Uhlig et al. Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2006; 70: 2058–2065.

Final Grade for Overall Quality of Evidence

Grade	Quality of Evidence	Meaning
A	High	The Work Group is confident that the true effect lies close to that of the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very Low	The estimate of effect is very uncertain, and often will be far from the truth.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction

Data extraction was done by the Evidence Review Team (ERT). The ERT, in consultation with the Work Group, designed forms to capture data on design, methodology, sample characteristics, interventions, comparators, outcomes, results, and limitations of individual studies. Methodology and outcomes were also systematically graded (see the section on grading below) and recorded during the data extraction process.

Summary Tables

Summary tables were developed for each comparison of interest (see Table 9 in the original guideline document). Studies included in the evidence base for the *KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease* were also incorporated if they fulfilled the inclusion criteria for the current Kidney Disease: Improving Global Outcomes (KDIGO) Guideline.

Summary tables contain outcomes of interest, relevant population characteristics, description of intervention and comparator, results, and quality grading for each outcome. Categorical and continuous outcomes were summarized separately. Studies done exclusively in patients of a single race or ethnicity and studies reporting effect modifications by baseline urine protein level were annotated. Studies were also categorized by baseline proteinuria status in summary tables for the chronic kidney disease (CKD) with diabetes mellitus topic.

For studies not exclusively examining CKD population, only those reporting analysis by CKD subgroups were tabulated. Studies including both diabetes mellitus and non-diabetes mellitus populations were included in summary tables for the CKD without diabetes mellitus topic unless results of subgroup analysis by diabetes mellitus status was provided.

Work Group members proofed all summary table data and quality assessments. Summary tables are available at www.kdigo.org (see the "Availability of Companion Documents" field).

Evidence Profiles

Evidence profiles were constructed to assess the quality and record quality grades and descriptions of effect for each outcome across studies, as well as the quality of overall evidence and description of net benefits or harms of the intervention or comparator across all outcomes. These profiles aim to make the evidence synthesis process transparent. Decisions in the evidence profiles were based on data from the primary studies listed in corresponding summary tables and on judgments of the ERT and the Work Group. When the body of evidence for a particular comparison of interest consisted of only one study, the summary table provided the final level of synthesis and an evidence profile was not generated. Evidence profiles were also not created for studies that did not exclusively examine CKD population. Each evidence profile was initially constructed by the ERT and then reviewed, edited, and approved by the Work Group. The work products created by the ERT for summarizing the evidence base are listed in Table 9 in the original guideline document.

Grading of Quality of Evidence for Outcomes of Individual Studies

Methodological Quality

Methodological quality (internal validity) refers to the design, conduct, and reporting of outcomes of a clinical study. A previously devised three-level classification system for quality assessment was used to grade the overall study quality and quality of all relevant outcomes in the study (see Table 10 in the original guideline document). Variations of this system have been used in most Kidney Disease Outcomes Quality Initiative (KDOQI) and all KDIGO guidelines and have been recommended for the US Agency for Healthcare Research and Quality Evidence-based Practice Center program.

Each study was given an overall quality grade based on its design, methodology (randomization, allocation, blinding, definition of outcomes, appropriate use of statistical methods, etc.), conduct (dropout percentage, outcome assessment methodologies, etc.) and reporting (internal consistency, clarity, thoroughness and precision, etc.). Each reported outcome was then evaluated and given an individual grade depending on the quality of reporting and methodological issues specific to that outcome. However, the quality grade of an individual outcome could not exceed the quality grade for the overall study.

Grading the Quality of Evidence and the Strength of a Guideline Recommendation

A structured approach, based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and facilitated by the use of evidence profiles was used to grade the quality of the overall evidence and the strength of recommendations. For each topic, the discussion on grading of the quality of the evidence was led by the ERT. The 'quality of a body of evidence' refers to the extent to which confidence in an estimate of effect is sufficient to support a particular recommendation.

Grading the Quality of Evidence for Each Outcome across Studies

Following GRADE, the quality of a body of evidence pertaining to a particular outcome of interest was initially categorized on the basis of study design. For questions of interventions, the initial quality grade was 'High' if the body of evidence consisted of randomized controlled trials (RCTs), 'Low' if it consisted of observational studies, and 'Very Low' if it consisted of studies of other study designs. For questions of interventions, the Work Group decided to use only RCTs. The grade for the quality of evidence for each intervention–outcome pair was then lowered if there were serious limitations to the methodological quality of the aggregate of studies, if there were important inconsistencies in the results across studies, if there was uncertainty about the directness of evidence including limited applicability of the findings to the population of interest, if the data were imprecise (a low event rate in either arm or a confidence interval [CI] spanning a range >1) or sparse (only 1 study or total N <500), or if there was thought to be a high likelihood of bias. The final grade for the quality of the evidence for an intervention–outcome pair could be one of the following four grades: 'High', 'Moderate', 'Low' or 'Very Low' (see "Rating Scheme for the Strength of the Evidence" field).

Grading the Overall Quality of Evidence

The quality of the overall body of evidence was then determined on the basis of the quality grades for all outcomes of interest, taking into account explicit judgments about the relative importance of each outcome. The resulting four final categories for the quality of overall evidence were: 'A', 'B', 'C', or 'D' (see the "Rating Scheme for the Strength of the Evidence" field).

See the original guideline document for additional discussion of assessment of net health benefit across all important clinical outcomes, ungraded statements, and the format for guideline recommendations.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Overview of Process

The Work Group, Kidney Disease: Improving Global Outcomes (KDIGO) Co-Chairs, Evidence Review Team (ERT), and KDIGO support staff met for three 2-day meetings for training in the guideline development process, topic discussion, and consensus development.

Commissioning of Work Group and ERT

The KDIGO Co-Chairs appointed the Work Group Co-Chairs, who then assembled the Work Group of domain experts, including individuals with expertise in internal medicine, adult and pediatric nephrology, cardiology, hypertension, pharmacology, epidemiology, and endocrinology. The Tufts Center for Kidney Disease Guideline Development and Implementation at Tufts Medical Center in Boston, Massachusetts, USA, was contracted to conduct systematic evidence review and provide expertise in guideline development methodology. The ERT consisted of physician–methodologists with expertise in nephrology, a project coordinator and manager, and a research assistant. The ERT instructed and advised Work Group members in all steps of literature review, critical literature appraisal, and guideline development. The Work Group and the ERT collaborated closely throughout the project.

Defining Scope and Topics

The Work Group Co-Chairs first defined the overall scope and goals of the guideline and then drafted a preliminary list of topics and key clinical questions. The Work Group and ERT further developed and refined each topic and specified screening criteria, literature search strategies, and data extraction forms (see Table 5 in the original guideline document).

Given the lack of robust evidence, the Work Group decided not to make guideline recommendations for patients with kidney failure (CKD 5D). The Work Group decided instead to refer readers to the KDIGO Controversies Conference paper on this topic.

Establishing the Process for Guideline Development

The ERT performed literature searches and organized abstract and article screening. The ERT also coordinated the methodological and analytical processes and defined and standardized the methodology for performing literature searches, data extraction, and summarizing the evidence. Throughout the project, the ERT offered suggestions for guideline development and led discussions on systematic review, literature searches, data extraction, assessment of quality and applicability of articles, evidence synthesis, grading of evidence and guideline recommendations, and consensus development. The Work Group took the primary role of writing the recommendation statements and rationale and retained final responsibility for their content.

The Work Group Co-Chairs prepared the first draft of the scope of work document as a series of open-ended questions to be considered by Work Group members. At their first 2-day meeting, members added further questions until the initial working document included all topics of interest to the Work Group. The inclusive, combined set of questions formed the basis for the deliberation and discussion that followed. The Work Group strove to ensure that all topics deemed clinically relevant and worthy of review were identified and addressed.

Formulating Questions of Interest

Questions of interest were formulated according to the PICODD (Population, Intervention, Comparator, Outcome, study Design and Duration of follow-up) criteria. Details of the criteria are presented in Table 5 in the original guideline document.

Ranking of Outcomes

The Work Group ranked outcomes of interest on the basis of their importance for informing clinical decision making (see Table 6 in the original guideline document). Doubling of serum creatinine (SCr) level or halving of glomerular filtration rate (GFR) was upgraded from 'high' to 'critical' importance in studies where the baseline GFR was < 60 ml/min/1.73 m^2 (or the SCr was >2 mg/dl [>177μmol/l]), given the known adverse consequences of advanced CKD.

Grading the Quality of Evidence and the Strength of a Guideline Recommendation

A structured approach, based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and facilitated by the use of

evidence profiles was used to grade the quality of the overall evidence and the strength of recommendations. For each topic, the discussion regarding the strength of the recommendations was led by the Work Group Co-Chairs.

The 'strength of a recommendation' indicates the extent to which one can be confident that adherence to the recommendation will do more good than harm.

Rating Scheme for the Strength of the Recommendations

Nomenclature and Description for Grading Recommendations

	Implications		
Grade[a]	**Patients**	**Clinicians**	**Policy**
Level 1 'The Work Group recommends'	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2 'The Work Group suggests'	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require debate and involvement of stakeholders before policy can be determined.

[a]The additional category 'Not Graded' was used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence. The most common examples include recommendations regarding monitoring intervals, counseling, and referral to other clinical specialists. The ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than Level 1 or 2 recommendations.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline draft was sent for peer review to the Kidney Disease: Improving Global Outcomes (KDIGO) Board of Directors in December 2010 and for public review in July 2011.

Review of Guideline Development Process

Several tools and checklists have been developed to assess the quality of the methodological process for guideline development. These include the Appraisal of Guidelines for Research and Evaluation (AGREE) criteria, the Conference on Guideline Standardization (COGS) checklist, and the Institute of Medicine's recent *Standards for Systematic Reviews*, and *Clinical Practice Guidelines We Can Trust*. Table 17 in the original guideline document and Supplementary Appendix 2 online (see the "Availability of Companion Documents" field) show, respectively, the COGS criteria and the Institute of Medicine standards, and how each one of them is addressed in this Guideline.

Comparison with Other Guidelines

The Work group tabulated recommendations from other key English-language guidelines pertinent to the use of blood-pressure lowering agents in individuals with chronic kidney disease (CKD) (see Table 16 in the original guideline document). This served to inform topic selection and scope. Also, after recommendations had been drafted, the Work Group reviewed them in the context of the existing guideline recommendations to avoid

unnecessary or unwarranted discrepancies.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of blood pressure in patients with chronic kidney disease

Potential Harms

Potential adverse effects generic to treatment used to lower blood pressure include decreases in cerebral perfusion (contributing to dizziness, confusion and falls) and acute deterioration in kidney function

Specific side effects of medications, of combinations of medications, and in specific populations are provided in Chapters 3-8, in summary tables and evidence profiles, and discussed in the rationale for each guideline statement in the original guideline document.

Contraindications

Contraindications

- Triamterene and amiloride are usually avoided in patients with chronic kidney disease (CKD) because of the risk of hyperkalemia.
- It is wise to avoid dihydropyridine calcium channel blockers in CKD patients with already increased urinary albumin excretion, particularly if there is not concomitant use of an angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB).
- Since clonidine can slow pulse rate, this drug should be avoided if bradycardia or heart block is present.

Qualifying Statements

Qualifying Statements

Use of the Clinical Practice Guideline

This Clinical Practice Guideline document is based upon systematic literature searches last conducted in January 2011, supplemented with additional evidence through February 2012. It is designed to provide information and assist decision making. It is not intended to define a standard of care, and should not be construed as one, nor should it be interpreted as prescribing an exclusive course of management. Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health-care professional making use of these recommendations is responsible for evaluating the appropriateness of applying them in any particular clinical situation. The recommendations for research contained within this document are general and do not imply a specific protocol.

Limitations

In children with chronic kidney disease (CKD), there is a dearth of randomized controlled trials; in fact, the recommendations in this chapter are

largely based on a single trial, ESCAPE, which limits the quality of the evidence and the strength of the recommendations. The ESCAPE trial was performed in a predominantly Caucasian population. Therefore, the generalization of these findings to other populations is uncertain.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney Int Suppl. 2012 Dec;2(5):337-414. [453 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2004 May (revised 2012 Dec)

Guideline Developer(s)

Kidney Disease: Improving Global Outcomes - Nonprofit Organization

Source(s) of Funding

Kidney Disease: Improving Global Outcomes (KDIGO) is supported by the following consortium of sponsors: Abbott, Amgen, Bayer Schering Pharma, Belo Foundation, Bristol-Myers Squibb, Chugai Pharmaceutical, Coca-Cola Company, Dole Food Company, Fresenius Medical Care,

Genzyme, Hoffmann-LaRoche, JC Penney, Kyowa Hakko Kirin, NATCO—The Organization for Transplant Professionals, NKF-Board of Directors, Novartis, Pharmacosmos, PUMC Pharmaceutical, Robert and Jane Cizik Foundation, Shire, Takeda Pharmaceutical, Transwestern Commercial Services, Vifor Pharma, and Wyeth. No funding is accepted for the development or reporting of specific guidelines. All stakeholders could participate in open review.

Guideline Committee

Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

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Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis 2004 May;43(5 Suppl 1):S1-290.

Guideline Availability

Electronic copies of the guideline: Available from the Kidney Disease: Improving Global Outcomes (KDIGO) Web site .

Availability of Companion Documents

The following are available:

- KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Appendices 1-2. New York: Kidney Disease: Improving Global Outcomes; 2012 Dec. 12 p. Electronic copies: Available in Portable Document Format (PDF) from the Kidney Disease: Improving Global Outcomes (KDIGO) Web site .
- KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Online supplemental tables. New York: Kidney Disease: Improving Global Outcomes; 2012 Dec. 127 p. Electronic copies: Available in PDF from the KDIGO Web site .
- Methods for development of KDIGO clinical practice guidelines. Electronic copies: Available from the KDIGO Web site .

Patient Resources

None available

NGC Status

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